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M. Saito

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF :  
HIROTOSHI ISHIDA ET AL : GROUP ART UNIT: 1761  
SERIAL NO: 09/581,180 :  
FILED: JULY 14, 2000 : EXAMINER: WONG  
FOR: GRANULAR SWEETENER :

RECEIVED  
TC 1100-A MAIL ROOM  
SEP 20 2002

DECLARATION UNDER 37 C.F.R. §1.132

ASSISTANT COMMISSIONER FOR PATENTS

WASHINGTON, D.C. 20231

SIR:

Now comes Yuichi SUZUKI, who deposes and states that:

1. That I am a graduate of Tohoku University and received my Master's degree in Chemical Engineering in the year 1997.
2. That I have been employed by Ajinomoto Co., Inc., the assignee of the above-identified application, for 5 years as a researcher in the field of Amino-science.
3. That I am a named inventor of the above-identified application.
4. That the following experiments were carried out by me or under my direct supervision and control.

I. Determination of the Solubility of Unmodified Powders and Single-Component Granules:

A 1L dissolution tester (the Japanese Pharmacopoeia, Paddle method (container of 100 mm in inner size, 160 mm in height, having a hemispheric bottom of 50 mm in radius, and a net volume of 1,000 ml; paddle formed by sectioning a disc

of 83 mm in size, and 3 mm in thickness, with parallel strings of 42 mm and 75 mm in length; 25 mm in distance between the lower end thereof and the container bottom), 100 rpm) was used together with 900 ml of water (20°C), in which 1 g of a sample was placed and examined for the time period required for dissolution (the endpoint being judged visually).

An Aspartame (APM) unmodified powder (having an average particle size of about 15 µm and a maximum particle size being about 100 µm; IB-type bundle-like crystals) and an Acesulfame-K (ACE-K) unmodified powder (having an average particle size of about 250 µm and a maximum particle size of about 500 µm) were used as samples both: (1) directly as they were; and (2) after having been granulated according to the method described below in II, followed by sieving into various mesh size fractions.

The time periods (min) required for dissolution were determined, and the results are shown below in Table 1.

Table 1: Time period for dissolution (min)

Sample particle size	APM	ACE-K
Original powder	30	3
Granule 500 to 1,400 µm	32	3
300 to 500 µm	18	2
100 to 500 µm	18	2
to 100 µm	29	3

## II. Preparation of granules of a mixture of APM and ACE-K:

The same ACE-K used in I (having an average particle size of about 250 µm and a maximum particle size being about 500 µm) was pulverized by a compact laboratory centrifugal pulverizer (250 µm φ screen, 20,000 rpm) to obtain a pulverized ACE-K product with an average particle size of about 20 µm and a

maximum particle size of about 250  $\mu\text{m}$ .

This pulverized ACE-K product was mixed with the same APM used in I (having an average particle size of about 15  $\mu\text{m}$  and a maximum particle size of about 100  $\mu\text{m}$ ) at various ratios and each resultant mixture was granulated using a dry roll mill (dry compaction and disintegration) and sieved to obtain fractions of granules of the mixture of APM and ACE-K having a varying particle size. Specifically, the dry compaction and the dry disintegration were performed using a compacting machine "ROLLER COMPACTER Model WP90 X30" (ex TURBO KOGYO), and the mixture was, upon compaction, fed to the compacting machine via a screw feeder (88 rpm) under a roll pressure of 4.9 Mpa at a roll speed of 12 rpm, and then disintegrated using a fine granulator screen of 12 mesh size (pore size being 1,400  $\mu\text{m}$ ). The granules were sieved using a JIS (Japanese Industrial Standard) standard sieve.

The thus-obtained granules of the mixtures of APM and ACE-K having various mixing ratios and various particle sizes were used for the tests described below in III.

### III. Solubility of Granules of a Mixture and a Mixture of Granules:

The samples of granules of mixtures were prepared by the method described above in II, using the same unmodified powders as employed in I. Analogous mixtures of granules were prepared by gently mixing with a spatula APM granules of a certain particle size and ACE-K granules of a certain particle size as referred to in I at a certain ratio.

The time periods required for dissolution of the granules were determined as described above in I. In greater detail, the time period required for dissolution were determined for the various granules of mixtures of APM and ACE-K (granules of mixture) and mixtures of APM granules and ACE-K granules (mixture of

granules) with the varying mixing ratios (ACE-K content) and particle sizes. 1 g of each sample was used in each trial. The results will be shown in Table 2 below.

Table 2: Time periods for dissolution (min)

Ratio of ACE-K present (% by weight)	5		20		50		90 (*1)	
	Particle size ( $\mu\text{m}$ )	Granules of mixture	Mixture of granules	Granules of mixture	Mixture of granules	Granules of mixture	Mixture of granules	Granules of mixture
500 to 1,400	27	33	24	31	13	25		
300 to 500	8	17	11	17	4	13		
100 to 300	6	16	4	18	3	15	4	
to 100	27	32	5	27	4	22		24

\*1 = Values in this column (as well as the original date for ACE-K 5% and 50%) were of non-sieved granules of a mixture or a mixture of granules.

#### IV. Conclusions:

By mixing and granulating Aspartame (APM) and Acesulfame-K (ACE-K) according to the invention, the poor solubility (i.e., poor dissolution speed) of APM can be improved markedly, and a sweetener having an excellent sweetness profile can readily be prepared.

As clearly shown by the results presented in Table 2, the dissolution rate of the granules of a mixture of APM and ACE-K is greater than that of a corresponding mixture of granules over a wide range of APM to ACE-K weight ratios and over a wide range of particle sizes.

In greater detail, for example, for mixtures which contain 5 % by weight of ACE-K and 95 % by weight of APM and having a particle size of 500 to 1,400  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 27 minutes, while the mixture of granules exhibits a dissolution rate of 33 minutes.

Similarly, for mixtures which contain 5 % by weight of ACE-K and 95 % by weight of APM and having a particle size of 300 to 500  $\mu\text{m}$ , the granules of a

mixture exhibit a dissolution rate of 8 minutes, while the mixture of granules exhibits a dissolution rate of 17 minutes,

For mixtures which contain 5 % by weight of ACE-K and 95 % by weight of APM and having a particle size of 100 to 300  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 6 minutes, while the mixture of granules exhibits a dissolution rate of 16 minutes.

For mixtures which contain 5 % by weight of ACE-K and 95 % by weight of APM and having a particle size of up to 100  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 27 minutes, while the mixture of granules exhibits a dissolution rate of 32 minutes.

For mixtures which contain 20 % by weight of ACE-K and 80 % by weight of APM and having a particle size of 500 to 1,400  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 24 minutes, while the mixture of granules exhibits a dissolution rate of 31 minutes.

For mixtures which contain 20 % by weight of ACE-K and 80 % by weight of APM and having a particle size of 300 to 500  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 11 minutes, while the mixture of granules exhibits a dissolution rate of 17 minutes,

For mixtures which contain 20 % by weight of ACE-K and 80 % by weight of APM and having a particle size of 100 to 300  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 4 minutes, while the mixture of granules exhibits a dissolution rate of 18 minutes.

For mixtures which contain 20 % by weight of ACE-K and 80 % by weight of APM and having a particle size of up to 100  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 5 minutes, while the mixture of granules exhibits a dissolution rate of 27 minutes.

For mixtures which contain 50 % by weight of ACE-K and 50 % by weight of

APM and having a particle size of 500 to 1,400  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 13 minutes, while the mixture of granules exhibits a dissolution rate of 25 minutes.

For mixtures which contain 50 % by weight of ACE-K and 50 % by weight of APM and having a particle size of 300 to 500  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 4 minutes, while the mixture of granules exhibits a dissolution rate of 13 minutes,

For mixtures which contain 50 % by weight of ACE-K and 50 % by weight of APM and having a particle size of 100 to 300  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 3 minutes, while the mixture of granules exhibits a dissolution rate of 15 minutes.

For mixtures which contain 50 % by weight of ACE-K and 50 % by weight of APM and having a particle size of up to 100  $\mu\text{m}$ , the granules of a mixture exhibit a dissolution rate of 4 minutes, while the mixture of granules exhibits a dissolution rate of 22 minutes.

For non-sieved mixtures which contain 90% by weight of ACE-K and 10% by weight of APM, the granules of a mixture exhibit a dissolution rate of 4 minutes, while the mixture of granules exhibits a dissolution rate of 24 minutes.

The improved dissolution rate for granules of mixtures of APM and ACE-K as compared to mixtures of granules of APM and ACE-K is practically significant. As explained on page 3 of the specification, the slow dissolution rate of APM is a significant problem in the use of APM for the manufacture of low-calorie soft drinks. An improvement in the dissolution rate of APM provides an improvement in the process of producing such soft drinks.

The improved dissolution rate for granules of mixtures of APM and ACE-K as compared to mixtures of granules of APM and ACE-K could not have been expected based on the prior art. There is no teaching in the prior art which would

have suggested that granules of a mixture of APM and ACE-K would exhibit an improved dissolution rate as compared to analogous mixtures of granules of APM and ACE-K.

5. I declare further that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

6. Further Declarant saith not.

Yuichi Suzuki  
Yuichi SUZUKI

March 13, 2002  
Date